Environmental Enrichment

NTP Board of Scientific Counselors Meeting

December 15, 2011

Presenter: Dr. Angela-King Herbert, NTP Cellular and Molecular Pathology Branch

Background

Environmental enrichment has been described as any measure that promotes expression of species-specific natural behaviors and inhibits abnormal behaviors (Brinkman, 1996). The National Research Council recently updated the *Guide for the Care and Use of Laboratory Animals* (*Guide*, NRC, 2011). The *Guide* addresses environmental enrichment:

All animals should be housed under conditions that provide sufficient space as well as supplementary structures and resources required to meet physical, physiologic, and behavioral needs. Environments that fail to meet the animals' needs may result in abnormal brain development, physiologic dysfunction, and behavioral disorders (Garner 2005; van Praag et al. 2000; Würbel 2001) that may compromise both animal well-being and scientific validity. The primary enclosure or space may need to be enriched to prevent such effect An appropriate housing space or enclosure should also account for the animals' social needs. Social animals should be housed in stable pairs or groups of compatible individuals unless they must be housed alone for experimental reasons or because of social incompatibility...The primary aim of environmental enrichment is to enhance animal well-being by providing animals with sensory and motor stimulation, through structures and resources that facilitate the expression of species-typical behaviors and promote psychological well-being through physical exercise, manipulative activities, and cognitive challenges according to speciesspecific characteristics... Well-conceived enrichment provides animals with choices and a degree of control over their environment, which allows them to better cope with environmental stressors (Newberry 1995).

Sztainburg et al. (2010) showed that enrichment was beneficial for the psychological and physical well being of animals. Animals in enriched conditions show decreased levels of anxiety-like behaviors in classic anxiety tests such as the elevated plus maze and the light dark transfer test. Male mice housed in cages enriched with nesting material had lower urine corticosterone levels, increased thymus weights, and consumed less feed and water than mice in standard (non-enriched) cages (Van Loo et al., 2004). The authors concluded that providing nesting material for a long period of time, reduced stress and enhanced animal welfare.

Adrenocorticotropic hormones and corticosterone, markers of chronic stress, were significantly lower in individually housed rats with enriched cages, as compared to controls in non-enriched cages (Belz et al., 2003). Additionally the author noted that upon observation, enriched rats

appeared easier to handle during acclimation and experiments. Konkle et al (2010) showed that corticosterone levels in enriched Sprague Dawley and Long Evans rats returned to baseline quicker than the control non-enriched rats after a brief stressor.

Types of environmental enrichment include social and physical enrichment. Social enrichment allows animals to display social behaviors such as grooming, vocalization and play. Rats are very social animals and group housing is an excellent method for promoting social interaction. Although mice are not as social as rats, group housing also works well in female mice; male mice tend to fight when housed in groups unless introduced at weaning. Physical enrichment devices should be biologically relevant enrichment items that have intrinsic value and allow the animal to display species-appropriate behavior. One must recognize normal rodent behavior and distinguish that from stereotypical behaviors. Enrichment devices can help to decrease or alleviate stereotypical behaviors in the animals that may be associated with stress.

Rodents are nocturnal, and foraging and burrowing are part of their normal behavior. Mice and rats are thigmotactic; they prefer to be in close proximity to walls or other structures and dislike open spaces. They usually favor shelters (nest or other types of shelters); mice are nest builders, while rats prefer gnawing but will build a loosely constructed nest with the "right" materials. It has be shown that rats have a preference for paper strips as nesting material (Manser et al., 1998)

Several factors must be considered when moving forward with an environmental enrichment program. The enrichment devices must be compatible with the aims of the study. This is especially important in studies conforming to Good Laboratory Practice regulations. Enrichment devices should be analyzed for contaminants to prevent the introduction of confounding variables. Furthermore, enrichment devices must have minimal impact on husbandry practices and cleaning procedures. Devices that require excessive staff time and labor for incorporation into studies are not acceptable. Also, the enrichment item must have minimal impact on observation of animals. For example, the use of large amounts of nesting materials can result in mice building very intricate nests in which concealment of the animals becomes an issue. Care must be taken in toxicology studies to ensure that the enrichment device does not impact research results.

Environmental Enrichment in NTP Studies

Modifications to the NTP animal care and use program denote an important effort to include environmental enrichment in NTP rodent studies. These changes to include environmental enrichment enhance animal well being by providing sensory and motor stimulation can improve the quality of experimental data, allow animals to have choices and control over their environment, and fulfill recommendations of the *Guide* and the Association for Assessment and Accreditation of Laboratory Animal Care International guidelines.

The NTP has drafted guidelines for the use of enrichment devices in NTP studies. Per the guidelines, (1) all devices must be screened for contaminants prior to use, (2) nesting material shall be autoclaved or irradiated to prevent the introduction of microbes to the cages, (3) other types of devices must be sanitized or discarded after use, (4) all animals on the study including sentinels shall receive the enrichment device, and (5) staff training of the use the device and

importance of program is essential to ensure adherence. Testing laboratories must develop standard operating procedures (SOPs) to ensure that the devices are used consistently throughout the study.

Enrichment devices will be used in NTP dosed feed, dosed water, and gavage studies while the appropriate environmental enrichment for inhalation and dermal studies are being explored. As the NTP moves forward in incorporating environment enrichment in studies there must be a balance between the uses of these devices without compromising the scientific questions under study.

References

Belz EE, Kennell JS, Czambel RK, Rubin RT, Rhodes ME Environmental enrichment lowers stress-responsive hormones in singly housed male and female rats. Pharmacol Biochem Behav. 2003 Dec;76(3-4):481-6.

Brinkman C. Toys for the Boys: Environmental Enrichment for Singly Housed Adult Male Macaques (*Macaca fascicularis*) Lab Prim News. 1996 April;35(2) http://www.brown.edu/Research/Primate/lpn35-2.html#toy

Konkle AT, Kentner AC, Baker SL, Stewart A, Bielajew C. Environmental-enrichment-related variations in behavioral, biochemical, and physiologic responses of Sprague-Dawley and Long Evans rats. J Am Assoc Lab Anim Sci. 2010 Jul;49(4):427-36.

Manser CE, Broom DM, Overend P, Morris TH. Investigations into the preferences of laboratory rats for nest-boxes and nesting materials. Lab Anim. 1998 Jan;32(1):23-35.

National Research Council. Guide for the Care and Use of Laboratory Animals. 2011.

Sztainberg Y, Chen A. An environmental enrichment model for mice. Nat Protoc. 2010 Sep;5(9):1535-9. Epub 2010 Aug 12.

Van Loo PL, Van der Meer E, Kruitwagen CL, Koolhaas JM, Van Zutphen LF, Baumans V. Long-term effects of husbandry procedures on stress-related parameters in male mice of two strains. Lab Anim. 2004 Apr;38(2):169-77.